

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

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| Applicant's or agent's file reference 064016355354 | FOR FURTHER ACTION | See item 4 below |
| International application No. PCT/CA2004/002172 | International filing date (<i>day/month/year</i>) 21 December 2004 (21.12.2004) | Priority date (<i>day/month/year</i>) 23 December 2003 (23.12.2003) |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | |
| Applicant MOUNT SINAI HOSPITAL | | |

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|-------------------------------------|---|---|-----------|---------------------|--------------------------|------------|----------|-------------------------------------|-------------|--|-------------------------------------|------------|----------------------------|-------------------------------------|-----------|---|--------------------------|------------|-------------------------|--------------------------|-------------|--|-------------------------------------|--------------|---|
| 1. | This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a). | | | | | | | | | | | | | | | | | | | | | | | | |
| 2. | This REPORT consists of a total of 9 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead. | | | | | | | | | | | | | | | | | | | | | | | | |
| 3. | <p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 80%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | <input checked="" type="checkbox"/> | Box No. I | Basis of the report | <input type="checkbox"/> | Box No. II | Priority | <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | |
| 4. | The International Bureau will communicate this report to designated Offices in accordance with Rules 44 <i>bis</i> .3(c) and 93 <i>bis</i> .1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44 <i>bis</i> .2). | | | | | | | | | | | | | | | | | | | | | | | | |

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|---|---|--|---|-----------------------|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70 | <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">Date of issuance of this report 26 June 2006 (26.06.2006)</td> </tr> <tr> <td style="padding: 5px;">Authorized officer <div style="text-align: center; font-weight: bold;">Athina Nickitas-Etienne</div></td> </tr> <tr> <td style="padding: 5px;">e-mail: pt04@wipo.int</td> </tr> </table> | Date of issuance of this report 26 June 2006 (26.06.2006) | Authorized officer <div style="text-align: center; font-weight: bold;">Athina Nickitas-Etienne</div> | e-mail: pt04@wipo.int |
| Date of issuance of this report 26 June 2006 (26.06.2006) | | | | |
| Authorized officer <div style="text-align: center; font-weight: bold;">Athina Nickitas-Etienne</div> | | | | |
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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7/7

PCT
REC'D 18 MAY 2005

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing 11 May 2005 (11-05-2005)
(day/month/year)

Applicant's or agent's file reference
064016355354

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/CA2004/002172

International filing date (day/month/year)
21 December 2004 (21-12-2004)

Priority date (day/month/year)
23 December 2003 (23-12-2003)

International Patent Classification (IPC) or both national classification and IPC
IPC(7): C12Q-1/68; C12Q- 1/02; G01N-33/53, 33/574; A61K-45/00, 49/00; A61P-35/00

Applicant
MOUNT SINAI HOSPITAL ET AL

1. This opinion contains indications relating to the following items :

- | | |
|--|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the opinion |
| <input type="checkbox"/> Box No. II | Priority |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement. |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
Place du Portage I, C114 - 1st Floor, Box PCT
50 Victoria Street
Gatineau, Quebec K1A 0C9
Facsimile No.: 001(819)953-2476

Authorized officer

Michael W. De Vouge (819) 997-2952

International application No.
PCT/CA2004/002172

| Box No. I | Basis of this opinion |
|-----------|---|
| 1. | With regard to the language , this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item. |

4. Additional comments :

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

☐ the entire international application

☒ claim 40

because:

☐ the said international application, or the said claim Nos.

relate to the following subject matter which does not require an international preliminary examination (*specify*) :

☒ the description, claims or drawings (*indicate particular elements below*) or said claim 40
are so unclear that no meaningful opinion could be formed (*specify*) :

Claim 40 is not considered to meet the requirements of Article 6 (PCT) for clarity, in that the claim specifies markers of claim 29. However, claim 29 is directed to a method and no specific markers are recited therein. On the basis of this ambiguity, it is impossible to undertake a meaningful search of this claim, as the claim is considered to be part of Invention I only on the basis of its dependency on claim 29.

☐ the claims, or said claims Nos. are so inadequately supported
by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that :

the written form ☐ has not been furnished
 ☐ does not comply with the standard

the computer readable form ☐ has not been furnished
 ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Box No. IV

Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has :

☐ paid additional fees

☐ paid additional fees under protest

☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with

☒ not complied with for the following reasons :

The International Search Authority found multiple groups of inventions in this international application, as follows:

I. Claims 1-22, 28, 29, 38 (partial), 39, 40 (partial), 47(partial), 48, 49:

Methods, kits and diagnostic compositions for detecting and *in vivo* imaging endometrial markers associated with an endometrial disease, particularly endometrial cancer.

II. Claims 23-25, 38 (partial), 39, 40 (partial), 47(partial):

Methods and kits for assessing efficacy of a test agent for inhibiting endometrial cancer.

III. Claims 26, 38 (partial), 39, 40 (partial), 47(partial):

Methods and kits for inhibiting endometrial cancer in a subject.

IV. Claims 27, 38 (partial), 39, 40 (partial), 47(partial):

Methods and kits for assessing the endometrial cancer cell carcinogenic potential of a test compound.

V. Claims 30-37, 47(partial):

Markers identified by differential expression in endometrial samples that distinguish an endometrial phase or disease; kits thereof. The claimed markers are considered to be a distinct invention in that the markers are unlinked to any of the other inventions by dependency thereto. Consequently, it is held that the claims are directed to compounds not limited to a specific use.

VI. Claims 41-45:

Methods and kits for determining uterine endometrial receptivity and probability of successful implantation, monitoring effects of ovarian stimulation on uterine endometrial receptivity.

VII. Claim 46, 47 (partial):

Method of contraception by interrupting presence of endometrial marker; kit therefor.

The special technical feature linking the claims of Invention I is considered to be the development of a detectable relationship between expression of endometrial markers and disease, particularly cancer. Said feature was absent from the claims of Inventions II - VII.

4. Consequently, this opinion has been established in respect of the following parts of the international application :

☐ all parts

☒ the parts relating to claim Nos. 1-22, 28, 29, 38 (partial), 39, 47(partial), 48, 49

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. V **Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|-------------------------------|--------|--|-----|
| Novelty (N) | Claims | 28, 29, 39 | YES |
| | Claims | 1-22, 38 (partial), 47 (partial), 48, 49 | NO |
| Inventive step (IS) | Claims | 39 | YES |
| | Claims | 1-22, 28, 29, 38 (partial), 47 (partial), 48, 49 | NO |
| Industrial applicability (IA) | Claims | 1-22, 28, 29, 38 (partial), 39, 47 (partial), 48, 49 | YES |
| | Claims | None | NO |

2. Citations and explanations :

Reference is made to the following documents:

D1 - WO98/10291 A1 (CENTER FOR CLINICAL & BASIC RESEARCH (DK)) 12 March 1998
D2 - WO99/63115 A2 (REPROGEN INC (US)) 9 December 1999
D3 - WO99/63116 A2 (REPROGEN INC (US)) 9 December 1999
D4 - WO01/62959 A2 (PROCREA BIOSCIENCES INC (CA)) 30 August 2001
D5 - WO01/92338 A1 (THE BRIGHAM AND WOMEN'S HOSPITAL, INC (US); THE OHIO STATE UNIVERSITY (US)) 6 December 2001
D6 - SHAARAWY, M. & EL-SHARKAWY, S.A. 2001. Acta Oncol Vol. 40, No. 4, pages 513-518
D7 - KLEIN, A.K. et al. 2000. Gynecol Oncol Vol. 78, pages 352-355
D8 - WO00/16805 A1 (DIADEXUS LLC (US)) 30 March 2000

With regard to novelty:

Claims 1, 2, 5, 6, 8-10, 38 (partial), 47 (partial), 48 and 49 are not considered to meet the requirements for Article 33(2) PCT for novelty in view of document D1. Document D1 discloses biochemical markers of human endometrium for detection in association with hyperplasia, adenocarcinoma or proliferative phase of endometrium. These were detected by comparison of two-dimensional gel electropherograms of extracted proteins from normal controls and afflicted tissues. Assays that utilize nucleic acid probes or antibodies, as well as kits, are also envisaged. Identified polypeptide markers having SEQ ID NOs: 1, 11 and 5 directly correspond to marker proteins of the instant application having SEQ ID NOs: 15, 23 and 47. Thus, the art discloses methods for detecting one or more endometrial markers (polypeptides or polynucleotides) associated with endometriosis or proliferating endometrium by: detecting said markers in proteins extracted from a sample; and comparing detected amounts to those of a control. Because the instant description does not make a distinction between controls and standards (p.20, lines 23-24; p. 23, line 35 to p.24, line 2), it is held that control determinations and standards are essentially synonymous and therefore, that the art discloses a standard determination. Consequently, the claims as recited are not held to be distinguished from embodiments of the art.

Claims 1, 2, 5, 6, 8-17, 22, 47 (partial), 48 and 49 are not considered to meet the requirements for Article 33(2) PCT for novelty in view of document D2 or D3. Said documents disclose the upregulation of cathepsin S and prothymosin (respectively) in human endometriotic tissue xenografted into severe combined immunodeficiency (SCID) mice, as compared to xenografts of normal tissue. Marker levels were measured by RT-PCR, although the use of additional methods such as competitive immunoassay using labeled antibody, PCR-ELISA, imaging by electron spin resonance (ESR) or magnetic resonance imaging (MRI), and mass spectrometry are also envisaged. These methods are indicated as useful for the diagnosis of endometriosis, monitoring therapeutic treatment progress by time-course measurement and for testing of therapeutics. Kits comprising marker-specific antibodies are also disclosed. Thus, the art discloses methods for detecting one or more endometrial polynucleotide markers associated with endometriosis by:

continued in Supplemental Box...

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 8, 10, 38-40 and 47 do not meet the requirement of PCT Rule 6.4(a), in that a multiply-dependent claim (claim 3) may not serve as a basis for another multiply-dependent claim.

Claim 13 is not considered to meet the requirements of Article 6 (PCT) for clarity, in that the phrase "the polynucleotides" contributes ambiguity with regard to the scope of the claim. The instant claim is dependent on claim 12, which specifies that any polynucleotide must be mRNA. Thus, the subject matter of claim 13 must specify a method of mRNA detection as well, despite the presence of a valid antecedent basis for the expression "the polynucleotides".

Claims 38-40 are not considered to meet the requirements of Article 6 (PCT) for clarity, in that the instant claims are directed to methods of any preceding claim. However, claims 22 and 30-37 are not directed to methods.

Claim 40 is not considered to meet the requirements of Article 6 (PCT) for clarity, in that the claim specifies markers of claim 29. However, claim 29 is directed to a method and no specific markers are recited therein. On the basis of this ambiguity, it is impossible to undertake a meaningful search of this claim, as the claim is considered to be part of Invention I only on the basis of its dependency on claim 29. Moreover, its dependency on claim 30 indicates that the claim was intended to encompass methods that utilize any endometrial marker as functionally defined in claim 30. The application is held to provide sufficient clarity under Article 6 (PCT) and sufficiency of disclosure under Article 5 (PCT) for only a limited number of claimed embodiments. Consequently, the search has been restricted to methods that utilize markers recited in claim 38, namely those selected from the group of SEQ ID Nos: 1, 3, 6, 9, 11, 13, 15, 18, 21, 23, 26, 30, 33, 36, 38, 40, 42, 45 and 47, which represent markers listed in Table 1.

Claim 47 is not considered to meet the requirements of Article 6 (PCT) for clarity, in that no kit component is recited. Additionally, the instant claim is also recited as being dependent on methods of any preceding claim. However, claims 22 and 30-37 are not directed to methods.

An incorporation by reference, such as on page 101, lines 8-13 compromises PCT Rule 5.1(a)(ii) because information required to carry-out the invention is in the document referred to, but not within the text of the description.

The description does not comply with PCT Rule 5.1(a)(ii). Specifically, all documents referred to in the description must be available to the public. Reference to the document(s) on page 15, line 34, page 104, line 34 (DeSouza et al) and page 109, lines 14-16 (conference proceeding) must be deleted or replaced by a reference to a document available to the public.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/002172

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

detecting said markers in an extracted sample; and comparing detected amounts to those of a control. Because the instant description does not make a distinction between controls and standards (p.20, lines 23-24; p. 23, line 35 to p.24, line 2), it is held that control determinations and standards are essentially synonymous and therefore, that the art discloses a standard determination. Consequently, the claims as recited are not held to be distinguished from embodiments of the art.

Claims 1, 2, 5, 6, 8-17, 22, 47 (partial), 48 and 49 are not considered to meet the requirements for Article 33(2) PCT for novelty in view of document D4. Said document discloses markers for diagnosis, prognosis, grading or treatment of endometriosis that are differentially expressed in normal as opposed to diseased tissue. These markers include numerous known genes, which include: NADH dehydrogenase, hUCC1, paralemmin, citrate transport protein, HIF 1 α , ARNT, Glut-1, MnSOD, Gpx, ATP synthase, c-jun, Cx43, HSP70 and cox2. Methods of detection that utilize RT-PCR are exemplified, although methods of protein detection are also disclosed, as are kits comprising specific antibody to such markers. Because the instant description does not make a distinction between controls and standards (p.20, lines 23-24; p. 23, line 35 to p.24, line 2), it is held that control determinations and standards are essentially synonymous and therefore, that the art discloses a standard determination. Consequently, the claims as recited are not held to be distinguished from embodiments of the art.

Claims 1-5, 7-9, 11, 18, 47 (partial), 48 and 49 are not considered to meet the requirements for Article 33(2) PCT for novelty in view of document D5. This document discloses methods for diagnosis of endometrial precancers by measurement of PTEN expression, thereby offering an immunohistochemical marker for that disease. Such precancers are characterized by decreased expression of PTEN, a tumor suppressor gene. The use of kits comprising specific antibodies to detect PTEN in endometrial tissues is disclosed, as is detection of the loss of PTEN gene sequences by PCR amplification methods. Because the instant description does not make a distinction between controls and standards (p.20, lines 23-24; p. 23, line 35 to p.24, line 2), it is held that control determinations and standards are essentially synonymous and therefore, that the art discloses a standard determination. Consequently, the claims as recited are not held to be distinguished from embodiments of the art.

Claims 1-6, 8, 9, 19, 21 and 22 are not considered to meet the requirements for Article 33(2) PCT for novelty in view of document D6. This document discloses detection of elevated levels of vascular endothelial growth factor and endostatin in sera from patients with endometrial hyperplasia and endometrial cancer, as measured by competitive enzyme immunoassay using specific antibody reagents directed against said markers. The relationship between tumor stage and VEGF expression is specifically measured and compared, as is the degree of expression of VEGF in samples from untreated individuals, treated individuals and relapsing individuals. Because the instant description does not make a distinction between controls and standards (p.20, lines 23-24; p. 23, line 35 to p.24, line 2), it is held that control determinations and standards are essentially synonymous and therefore, that the art discloses a standard determination. Consequently, the claims as recited are not held to be distinguished from embodiments of the art.

Claims 1-6, 8, 9, 11-18, 20 and 22 are not considered to meet the requirements for Article 33(2) PCT for novelty in view of document D7. This document discloses that detection of cytokeratin 20 mRNA, a known marker for endometrial cancer, may be used to detect metastatic endometrial tumor-derived cells in human blood. Detection is achieved using RT-PCR of CK20 mRNA from blood samples. Because the instant description does not make a distinction between controls and standards (p.20, lines 23-24; p. 23, line 35 to p.24, line 2), it is held that control determinations and standards are essentially synonymous and therefore, that the art discloses a standard determination. Consequently, the claims as recited are not held to be distinguished from embodiments of the art.

Claims 28 and 29 are considered to meet the requirements of Article 33(2) PCT for novelty, in that no single prior art document appears to disclose an *in vivo* imaging method wherein a labeled agent is injected into a subject and said agent binds to an endometrial marker, thereby localizing the label to diseased endometrial tissue.

Claim 39 is considered to meet the requirements of Article 33(2) for novelty, as the prior art does not disclose or fairly suggest the use of chaperonin 10 as a marker for the detection of an endometrial disease or phase.

continued on following page...

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/002172

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Supplemental Box

With regard to inventive step:

Claims 3 and 4 are not considered to meet the requirements of Article 33(3) PCT for inventive step in view of any of documents D1 - D4. Further to the previous discussion with regard to novelty, these documents envisage but do not enable assays of endometrial markers that specifically bind thereto. However, a skilled artisan would be expected to generate suitable antibodies by methodologies well-known in the art. Thus, the instant claims are not considered to be inventive over said art.

Claims 28 and 29 are not considered to meet the requirements of Article 33(3) PCT for inventive step in view of any of documents D5-D7 in combination with document D8. Document D8 discloses methods for detecting gynecological cancers through the measurement of expression of a protein referred to as Pro104 (p.24, lines 20-23). Exemplary support included the testing of endometrial cancers, although a strong correlation between Pro104 expression and presence of endometrial cancer was not found. However, this document also discloses methods for *in vivo* imaging and the use of labeled antibodies to achieve said imaging. Consequently, one skilled in the art would be apply to apply the teachings of D8 with regard to imaging to antibody reagents of documents D5-D7 to obtain an *in vivo* method for imaging an endometrial marker.

Claim 39 is considered to meet the requirements of Article 33(3) PCT for inventive step.

With regard to industrial applicability:

Claims 1-22, 28, 29, 38 (partial), 39, 47 (partial), 48 and 49 are considered to meet the requirements of Article 33(4) PCT for industrial applicability.